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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/733,640	12/08/2000	Anthony J. McHugh	10322/8	2399

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EXAMINER	
GOLLAMUDI, SHARMILA S	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 11/14/2003

17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/733,640	MCHUGH ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 September 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,17-19,34,35,38 and 48-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,17-19,34,35,38 and 48-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *14* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt of the Information Disclosure Statement received on December 27, 2003 and Extension of Time and Amendment C received on September 23, 2003 is acknowledged. Claims **1-8, 17-19, 34-35, 38, and 48-59** are pending in this application.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-3, 5-6, 34, 38-49, 51, 52, 59 are rejected under 35 U.S.C. 102(a) as being anticipated by McHugh et al (Phase Inversion Dynamics Of PGLA Solutions Related To Drug Delivery, Mat. Res. Soc. Symp. Proc. 550:41-46 1999).

McHugh et al disclose an injectable depot containing PLGA (crystallizable polymer), PVP (amorphous polymer), NMP (biocompatible solvent), triacetin (component solvent), and a bioactive agent. See page 42. The reference teaches the method of making the composition.

Note PGLA utilized in the reference has the ability to crystallize into ordered morphology as seen in the phase conversion. Further compared to PVP, PGLA is more crystalline in nature.

Claims 1-3, 5, 6, 8, 34, 38, 48-49, 51-52, 54, and 58-59 are rejected under 35 U.S.C. 102(b) as being anticipated by Brodbeck et al (Journal of Controlled Release 62 (1999) 333-344).

Brodbeck et al disclose two-phase gelled implant and drug release from a polymeric system (injectable depot). The system contains a biodegradable polymer (PLGA), a bioactive agent, a solvent (ethyl benzoate, triacetin, NMP), and PVP (amorphous polymer). See page 334. The reference teaches the method of making the composition.

Note PGLA utilized in the reference has the ability to crystallize into ordered morphology as seen in the phase conversion. Further compared to PVP, PGLA is more crystalline in nature.

Claims 1-3, 5-6, 34, 38, 48-49, 51-52, and 58-59 are rejected under 35 U.S.C. 102(a) as being anticipated by Graham et al (Phase Inversion Dynamics Of PGLA Solutions Related To Drug Delivery; Journal of Controlled Release)

Graham et al disclose an injectable depot containing PLGA (crystallizable polymer), PVP (amorphous polymer), NMP (biocompatible solvent), triacetin (component solvent), and a bioactive agent. See page 236. The reference teaches the method of making the composition. Graham et al disclose the polymeric solution undergoes a liquid-liquid phase inversion to produce a two-phase gelled implant. See page 233.

Note PGLA utilized in the reference has the ability to crystallize into ordered morphology as seen in the phase conversion. Further compared to PVP, PGLA is more crystalline in nature.

Claims 1-3, 5-7,17, 34, 38, 48-49, 51-53, 55, and 59 are rejected under 35 U.S.C. 102(e) as being anticipated by Shukla (6,432,438).

Shukla teaches a biodegradable vehicle containing a drug, solvent (NMP and triacetin, two different polymers (PLGA and PCL), and polyol (PEG) that is injected into an organism (examples, esp. 29). The method of mixing the polymer, solvent, and drug are taught in examples. The reference teaches the blending of two different biodegradable polymers with varying crystallinity and amorphous states. See column 3, lines 60-65, column 9, lines 30-35, and examples.

Response to Arguments

Applicant argues that the only teaching of crystallinity in Shukla is broad and there are infinite possible combinations. Applicant argues that there is no specific teaching of a mixture of crystallizable and non-crystallizable polymers. It is argued that a genus does not anticipate a species when the species is an infinite amount.

Applicant's arguments have been fully considered but they are not persuasive. First the examiner points out that the independent claims are generic and do not specify the type of crystallizable polymers and amorphous polymers. Therefore, as recognized by the applicant, Shukla discloses the combination of varying crystallinity and amorphous states in example 29. It is pointed out that applicant has not distinguished over the prior art by stating the amount of crystallinity in the polymer. Further, it is

pointed that that crystallizable polymers have both amorphous regions at certain temperatures and after implantation undergo a phase change, the broad aspect of the claims do not address this. Therefore, the applicant's claims are not specific as argued. In response to the teaching of the species, the examiner points to example 29 wherein the combination of PLA:PCL is taught. The reference clearly states blending two polymers with different physical properties (crystallinity). PCL is a semi-crystalline polymer whereas PLGA is more amorphous in nature. In regards to PGLA, the reference teaches the different co-monomers ratios make it more or less crystalline.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 18 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shukla (6,432,438) by itself or in view of WO 00/19837.

As set forth above, Shukla teaches a biodegradable vehicle containing a drug, solvent, two different polymers (PLGA and PCL) that is injected into an organism (examples, esp. 29). The method of mixing the polymer, solvent, and drug are taught in examples. Shukla teaches the blending of different polymers or copolymers with different crystallinity can result in a biodegradable vehicle with different degradation rates. Further, Shukla teaches that amorphous polymers degrade quicker. Column 7, lines 19-50. The reference teaches several different polymers such as PLA and a mixture of polymers may be used to manipulate the degradation characteristics of the delivery system. See column 5, lines 26-40.

Shukla does not exemplify instant poly (D, L-lactic acid).

WO teaches that polylactic has two forms" PDLA and PLLA. WO teaches that the individual forms are highly crystalline and a mixture is poly(D, L-lactic acid), which is less crystalline or more amorphous depending on the monomer ratio. See page 6.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Shukla and WO. One would be motivated to add poly (D, L-lactic acid) in Shukla's system since WO teaches that the instant polymer is more amorphous. Therefore, one would be motivated to add instant polymer to change the degradation rate of the polymer vehicle since Shukla teaches that the combination of different crystalline polymers manipulates the release rate. The examiner points out that it is within the skill of the art to ascertain the crystallinity of a polymer; for instance a homopolymer is more crystalline than a polymer blend or

copolymer. Further, it is within the skill to change the monomer ratio of a copolymer to yield a more or less crystalline polymer.

Claims 4, 8, 19, 50, 54, and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shukla (6,432,438) in view of Brodbeck et al (6,130,200).

Shukla teaches a biodegradable vehicle containing a drug, solvent, two different polymers (PLGA and PCL) that is injected into an organism (examples, esp. 29). The method of mixing the polymer, solvent, and drug are taught in examples. Shukla teaches benzyl benzoate. See figure 1a.

Shukla does not teach instant solvent or emulsifying agent.

Brodbeck et al disclose a gel composition containing a biocompatible polymer, ethyl or benzyl benzoate, a biocompatible component solvent, a bioactive agent, and an emulsifier. (Note Examples, Tables 1-2) Brodbeck teaches biodegradable polymers include polylactides, polyglycolides, polyanhydrides, and polycaprolactone (col. 10, lines 65-68). Brodbeck teach a solvent having a solubility in water of less than 7% allows for suitable burst control and sustained release of the beneficial agent. Brodbeck teaches benzoic acid solvents are preferred because they provide increased control of water migration resulting in increased stability of the active agent. See column 14, lines 1-25). Emulsifying agents are taught for an injectable depot gel composition to manipulate the viscosity of the gel (col. 18, lines 10- 56 and Figure 3).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Shukla and Brodbeck and utilize the instant solvent and emulsifying agents. One would be motivated to use instant solvent

since the instant solvent has certain properties that provides stability for the active agent, as taught by Brodbeck. Further, one would be motivated to use an emulsifying agent to manipulate the viscosity of the composition. Therefore, one would be motivated to use an emulsifying agent to yield the desired consistency of the composition; for instance to allow administration of a viscous implant composition via a needle. One would expect similar results by combining the references since both reference teach controlled release via similar polymeric systems.

Claims 4, 7, 19, 53, and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over McHugh et al or Brodbeck et al or Graham et al in view of US patent 6,130,200 (Brodbeck et al).

McHugh et al, Brodbeck et al, and Graham et al teach an injectable depot with a biodegradable crystallizable polymer, amorphous polymer, solvent, and drug.

The references do not teach PCL as the polymer or the emulsifying agent.

Brodbeck et al disclose a gel composition containing a biocompatible polymer, ethyl or benzyl benzoate, a biocompatible component solvent, a bioactive agent, and an emulsifier. (Note Examples, Tables 1-2) Brodbeck teaches biodegradable polymers include polylactides, polyglycolides, polyanhydrides, and polycaprolactone (col. 10, lines 65-68). Brodbeck teach a solvent having a solubility in water of less than 7% allows for suitable burst control and sustained release of the beneficial agent col. 8, lines 48-60). Brodbeck teaches for the preferred polymer PLGA, benzoic acid solvents are preferred (col. 14, lines 1-6). The reference teaches the use of emulsifying agents to manipulate

the viscosity of the composition See Figure 3 and column 19, lines 5-10). Brodbeck also teaches an injectable gel composition (col. 18, lines 56).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the references and US patent and utilize the instant polymer. One would be motivated to utilize the instant polymer since Brodbeck teaches that PCL is also a biodegradable polymer that may be used in an injectable depot that forms an implant. One would expect similar results since both teach polymeric controlled release devices. Further, one would be motivated to use instant solvent since Brodbeck states that instant solvent has certain properties that allow controlled release of the active agent. Lastly, a skilled artisan would be motivated to add an emulsifying agent to manipulate the viscosity of the injectable composition as taught by US patent.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is (703) 305-2147. The examiner can normally be reached on M-F (7:30-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Sharmila Gollamudi
November 5, 2003

MICHAEL G. HARTLEY
PRIMARY EXAMINER